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07-566977

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United States Patent [19]
Cook et al.

[11] **Patent Number:** **5,623,065**
[45] **Date of Patent:** **Apr. 22, 1997**

[54] **GAPPED 2' MODIFIED OLIGONUCLEOTIDES**

[75] Inventors: Phillip D. Cook, Vista; Brett P. Monia, Carlsbad, both of Calif.

[73] Assignee: Isis Pharmaceuticals, Inc., Carlsbad, Calif.

[21] Appl. No.: 244,993

[22] PCT Filed: Dec. 23, 1992

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PCT Pub. Date: Jul. 8, 1993

Related U.S. Application Data

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[51] Int. Cl.⁶ C07H 21/00; C07H 21/02; C07H 21/04

[52] U.S. Cl. 536/23.1; 536/23.2; 536/23.5; 536/23.51; 536/23.52; 536/23.53; 536/25.1; 536/25.2; 435/91.1; 435/91.2; 435/91.5; 935/6; 935/9; 935/10

[58] Field of Search 514/44; 536/23.1, 536/23.2, 23.5, 23.51, 23.52, 23.53, 25.1, 25.2; 435/91.1, 91.2, 91.4, 91.5; 935/9, 6, 10

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[57] **ABSTRACT**

Oligonucleotides and other macromolecules are provided that have increased nuclease resistance, substituent groups for increasing binding affinity to complementary strand, and subsequences of 2'-deoxy-erythro-pentofuranosyl nucleotides that activate RNase H enzyme. Such oligonucleotides and macromolecules are useful for diagnostics and other research purposes, for modulating protein in organisms, and for the diagnosis, detection and treatment of other conditions